



United States
Department of
Agriculture

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CENTER FOR VETERINARY BIOLOGICS NOTICE NO. 02-17

Marketing and
Regulatory
Programs

Animal and Plant
Health Inspection
Service

Veterinary Services

Center for Veterinary
Biologics
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Subject: Replacement of the Center for Veterinary Biologics' Killed Veterinary Rabies Reference

To: Biologics Licensees, Permittees, and Applicants
Veterinary Services Management Team
Directors, Center for Veterinary Biologics

This notice provides information on the availability of a new lot of Killed Veterinary Rabies Reference, Lot 99-02. The reference is used in the National Institutes of Health (NIH) rabies potency test for killed veterinary rabies vaccines and replaces the previous Reference Lot 89-3-1.

The 4th edition of the World Health Organization's (WHO) *Laboratory Techniques in Rabies*, Chapter 37, The NIH Test for Potency, included by reference in Title 9, Code of Federal Regulations, Part 113, Section 209 (9 CFR 113.209), recommends that the national control authority periodically replace the reference vaccine used in the NIH rabies potency test and that the reference be calibrated against the international standard. The present reference has been in use since 1990, was never calibrated to the WHO standard, and has shown a gradual decline in potency over this period.

The Center for Veterinary Biologics (CVB) produced a challenge virus standard (CVS) reference vaccine by propagation of the virus in baby hamster kidney cells. The reference was beta-propiolactone inactivated and lyophilized. The reference is non adjuvanted. After initial testing and preliminary calibration, a cooperative study was conducted with five veterinary biologics firms comparing Reference Lot 89-3-1, Reference Lot 99-02, and the 5th WHO rabies reference vaccine. Based on the results of that study and the 50 percent effective dose (ED₅₀) of Reference Lot 89-3-1 during its use at the CVB, Reference Lot 99-02 was determined to be equivalent to the historical mean potency of Reference Lot 89-3-1. Each vial of Reference Lot 99-02 contains 28 international units (I.U.) or 1.4 I.U. per ml when reconstituted and diluted per recommendations.

Reference Lot 99-02 is available upon request from the CVB. Please follow the procedures outlined in Veterinary Services Memorandum 800.97 for requesting this reagent. Effective November 12, 2002, United States veterinary biologics manufacturers shall conduct the NIH test using Reference Lot 99-02. If a serial has already been tested with Reference Lot 89-3-1 before November 12, 2002, and subsequent testing is required, then that testing may be with Reference Lot 89-3-1. Reference Lot 99-02 may be used prior to November 12, 2002, at the veterinary biologics manufacturer's discretion.



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(Voice/TTY/ASCII/Spanish)
1-800-877-8339

Relative potency values presently in approved Outlines of Production shall be the release value when using Reference Lot 99-02. The reconstitution and dilution procedures to be followed are included with the Reference and Reagent sheet supplied with the reagent. The initial starting dilution of the reference shall be user determined and adequate to meet the relevant Code of Federal Regulations criteria and the criteria recommended in *Supplemental Assay Method for Potency Testing of Inactivated Rabies Vaccine in Mice Using the National Institutes of Health Test* (SAM 308). The previous Reference Lot 89-3-1 will remain available for a limited period of time for use in stability testing of product previously tested with that reference and for other testing needs.

/s/ Richard E. Hill, Jr.

Richard E. Hill, Jr.
Director
Center for Veterinary Biologics